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The Use of Electrophysiological and Cognitive Variables in the Assessment of Degradation During Periods of Sustained Wakefulness

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between 25 and 30 years of age served as subjects. Electrophysiological and cognitive data were recorded during one day of baseline, two consecutive days of sleep deprivation, and one day of recovery.

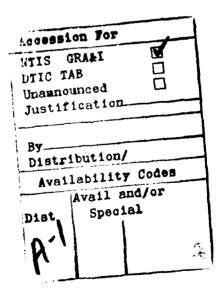


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Introduction

Army aviation personnel often encounter work schedules which require the transition from daytime to nighttime duty hours without the benefit of an adaptation period. Rotations from daytime to nighttime duty hours, particularly those that occur within a 24-hour period, usually result in loss of sleep, fatigue, and cognitive degradation (Comperatore and Krueger, 1990).

Strategies in the scheduling of sleep, meals, work, and exercise are currently under study with the purpose of identifying patterns that assist in the physiological adaptation to nighttime duty hours. These coping strategies are composed of countermeasures designed to prevent the sleep loss and chronic fatigue usually associated with rapid transitions from daytime to nighttime duty hours.

The study of shiftwork coping strategies requires the empirical characterization of effective countermeasures which prevent chronic fatigue and preserve normal cognitive function. In the laboratory, the study of variables such as alertness, sensory processing, reaction time, and cognitive processing allows the identification of effective countermeasures. This assessment approach requires the use of multidisciplinary test batteries that not only challenge cognitive processes, but also document the functional status of brain regions associated with sensory processing and alertness.

The aim of this study was to evaluate the usefulness of a test battery designed to characterize the state of alertness and cognitive ability of subjects involved in postponing sleep for approximately 60 consecutive hours. Three specific tests were included in this battery based on existing experimental evidence of their ability to reflect some aspect of alertness, sensory processing, and cognitive function.

Electrophysiological tests involving brain responses to auditory stimulation in the middle latency range and spectral analysis of resting electroencephalography (EEG) data were selected as two of three tests comprising the multidisciplinary battery. Resting EEG data provide indications of arousal state via analysis of relative and absolute power of spectral components. Spectral components were selected on the basis of their relation to states of alertness. In normal human adults, diffuse low frequency synchronized brain activity is associated with sleep (delta, 1.5 to 3.5 Hz; theta, 3.5 to 7.5 Hz), physical

relaxation and mental inactivity (alpha, 7.5 to 12.5 Hz), and drowsiness (theta) (Niedermeyer, 1987). In contrast to alpha and delta activity, theta activity can also be consistently observed over the frontal midline (F_z, C_z) during mental activities requiring concentration and attention (Ishihara and Yoshii, 1972) although increased beta activity is most often associated with mental activation. In general, the brain's electrical activity increases in amplitude and decreases in frequency as activation is reduced. Conversely, during heightened alertness, electrical activity decreases in amplitude and synchrony while simultaneously increasing in frequency (Greenfield & Sternbach, 1972).

Studies of human performance under schedules demanding extended hours of continuous work indicate that cognitive performance, such as number of problems solved and time spent searching for solutions, has been positively correlated with frontal and occipital energy in the 21-30 Hz range and negatively correlated with energy in the 1-3 Hz range (Nebylitsyn and Mozgovoy, 1973). Alpha (8-12 Hz) activity was shown to decrease in airmen during prolonged flights, in truck drivers after working 7-hour shifts, and in stenographers after working 6-hour shifts (Petrek, 1982). Other findings showed that theta (4-7 Hz) activity is often increased during states of discomfort such as weightlessness, acceleration, and sensory deprivation. addition, it was observed that theta (4-7 Hz) and delta (1-3 Hz) increased as subjects were exposed to increasing altitude conditions, and that these changes in the EEG were accompanied by increases in reaction time, decreases in working ability, deterioration of handwriting, and ultimately, loss of consciousness.

Belyavin and Wright (1987) reported that while EEG changes could not predict vigilance in a linear fashion, increased theta and delta activity and decreased beta activity were associated with performance degradation during 15 hours of testing. These results are consistent with the basic arousal hypothesis which suggests an increase of slow-wave EEG as a function of decreased alertness. Further consistent evidence has been offered by Pigeau, Heslegrave, and Angus (1987) who found that increased delta and theta activity were associated with increasing levels of sleep deprivation throughout a 64-hour deprivation period.

In addition to indications of alertness degradation obtained from spontaneous EEGs, experimentation with neural responses to auditory stimulation in sleeping subjects provides evidence of the functional status of alertness and sensory processing systems. Clinical and experimental data indicate that middle latency evoked responses (MLRs) are likely to reflect neural activity from cortical and subcortical substrates such as the thalamus, the temporal cortex, and the reticular formation (Buchwald et al., 1981; Comperatore et al., 1989; Woods et al., 1987; McGee et al., 1991; Spydell, Patte, Goldie, 1985).

The morphology of the MLR has been shown to vary as a function of alertness level. In human adults, two independent laboratories have shown that MLR components Pa (30 to 35 ms) and Nb (40 to 50 ms) exhibit latency increases while Pl (50 to 70 ms) is no longer detectable during slow wave sleep (Erwin and Buchwald, 1986; Osterhammel, Shallop, Terkildsen, 1985). cats, synchronized EEG activity in the delta range has been shown to be associated with a decrease in the unit firing rates in nuclei of the ascending mesencephalic reticular formation (Steriade et al., 1980, 1982; Erwin, 1986). Changes in the morphology of the Nb-Pl complex may not only occur during sleep, but may also occur in association with significant reductions of Thus, the MLR test was included in the multialertness. disciplinary test battery with the specific purpose of documenting changes in the neural activity of brain regions associated with alertness and the processing of sensory stimuli.

The third test component of the multidisciplinary battery assessed the status of cognitive function using the logical reasoning and manikin tasks from the Walter Reed Performance Assessment Battery (PAB). The manikin test has been shown to be sensitive to the effects of saturation diving on Navy divers, yet questions remain about the sensitivity of this test to other environmental stressors (Perez et al., 1987). Data on the sensitivity of the logical reasoning task are equivocal. The task has been shown to be sensitive to the effects of nitrogen narcosis (Baddely, 1968), diurnal variations in performance 'Englund, et al., 1985), and sleep loss (Angus, Heslegrave, and Myles, 1985; Haslam, 1982). However, Pleban, Thomas, and Thompson (1985) failed to detect sleep loss effects on logical reasoning.

The use of this test battery (MLR-EEG-PAB) permitted the concurrent evaluation of sensory processing, alertness, and cognitive function in single sessions. Extreme fatigue was expected to cause significant changes from presleep deprivation values in electrophysiological (MLR and EEG) and cognitive (LR and MR) variables. Deterioration of MLR amplitude, increased EEG synchronization, increased PAB reaction times, and reductions in PAB correct responses were expected to converge when subjects lost the ability to compensate for the deleterious effects of fatigue on CNS and cognitive function.

At low fatigue levels only CNS changes were expected to vary as a demonstration of fatigue indicating that subjects were experiencing CNS degradation but were able to compensate and preserve normal cognitive function. Therefore, we hypothesized that if the test profile successfully assessed CNS and cognitive function, electrophysiological and cognitive measurements would exhibit somewhat independent patterns of degradation as a function of sustained wakefulness. Convergence in the degradation patterns was expected to occur only at times in which subjects were overcome by fatigue and unable to compensate for the decrease in alertness.

Methods

Subjects

Eight male volunteers between 25 and 30 years of age served as subjects. Consent forms were signed by participants and witnessed by an uninterested observer. Consent forms contained a detailed description of objectives and procedures. Participation was voluntary and withdrawal from the study was possible at any time without penalty.

A flight surgeon stationed at the U.S. Army Aeromedical Research Laboratory's (USAARL) Biomedical Application Research (BAR) Division served as the medical monitor. Throughout the study the medical monitor was either in the facility or on call. Prior to the beginning of the study, the medical monitor conducted a physical examination of each potential subject. Participants were excluded if they exhibited any of the following characteristics: current illness, blood pressure greater than 140/90, current use of benzodiazepine compounds, tranquilizers, or antidepressants, history of impaired renal or hepatic function, pulmonary insufficiency, organic heart disease, sleep disorder, inpatient psychiatric therapy, or hearing loss above 25 dB [ANSI S3.6-1969 (R1973)].

Participants were asked to suspend consumption of caffeine-containing beverages 2 days prior to the beginning of the experiment; the consumption of alcoholic beverages and stimulants throughout the experiment was also prohibited. Trips out of the Laboratory were permitted under the supervision of a member of the research team.

Throughout the entire study, subjects were under the constant supervision of staff members. Subjects had one mandatory physical exercise period prior to the 1300 to 1500

hour test session which consisted of walking, running, and weight lifting. After the 2200 hour test session, subjects were encouraged to walk outside the testing facility for approximately 30 minutes. Outdoor walks were allowed during the night without restriction. Inside activities included the use of a UH-1 flight simulator, computer games, video tapes, and cable television.

At the end of the sleep deprivation period, subjects were required to sleep from 2200 h to approximately 1100 h of the next morning. At the conclusion of the study, subjects were advised that they may experience drowsiness and fatigue and should avoid driving or operating complex or dangerous equipment during the next 48 hours. Subjects were then driven to their residence by a relative or a staff member and were advised to resume their normal sleep schedule.

Apparatus

Electrophysiological data were collected using 21 channels of a Cadwell Spectrum-32 brain mapping unit. In all cases, 18 Ag-AgCl Grass electrodes (F_7 , F_3 , F_2 , F_4 , F_8 , F_3 , F_5 , F_4 , F_6 , F_6 , F_7 , F_8 ,

General procedure

Participants initially reported to the USAARL facility on Monday at 0700 hours. This day was used to train and familiarize subjects with the experimental procedures associated with this study. A training schedule was followed throughout the adaptation day which culminated with a scheduled bedtime at 2400 (Table 1). Electrophysiological and cognitive data were recorded during 1 day of baseline, 2 consecutive days of sleep deprivation, and 1 day of recovery. Subjects were tested in

groups of two or three--two groups of three subjects and one group of two subjects.

During baseline nights and the night of the second day of deprivation, subjects were allowed to sleep and were encouraged to go to bed no later than 2400. The same procedures were used for data acquisition during baseline, sleep deprivation, and recovery days. The chronological sequences of these tests are described in these three tables: Table 2 for baseline (day 1), Table 3 for sleep deprivation (days 2 and 3), and Table 4 for recovery (day 4).

Recording of baseline EEG endogenous activity

EEG rhythms were recorded under laboratory conditions from all eight subjects. Subjects were seated in a reclining chair located in a sound-attenuated room adjacent to the EEG recording equipment. EEG data were recorded during two 5-minute periods in which subjects were instructed to sit quietly and relax with eyes open looking at a fixation point placed 5 feet away from them. The lowpass filter was set at 100 Hz with a time constant of 0.30 s.

Recording of middle latency responses

Middle latency evoked responses were obtained from all eight subjects under controlled conditions. Subjects were asked to sit comfortably in a reclining chair located within a soundproof room. Prior to each recording session, subjects were instructed to relax and to look at a red dot located 5 feet away at eye level. MLR data were recorded from 21 sites on the scalp identified in the International 10-20 system (Jasper, 1958).

MLRs were recorded in response to 40 dB HL binaural rarefaction click stimuli delivered at a rate of 1.1/s through insert earphones. Responses were filtered from 1-1000 Hz (48 dB/octave). The sampling time of the signal averager (Cadwell-Spectrum 32) was 100 milliseconds of poststimulus time. The acquisition sampling rate was 100 kHz. The amplitude and latency of the brainstem response visible in the 100 ms window was monitored continuously in order to guard against accidental displacement of the earphones. Averaged responses (200) were stored in digital form for later analysis.

Cognitive function

Subjects were presented with two cognitive performance tests, one requiring mental rotation of a manikin figure, and a second task requiring the use of logical reasoning. During the mental rotation task, the subject was first presented with a manikin of a human figure which stood either inside a circle or a In either case, the manikin held a square in one hand and a circle in the other hand. The task consisted of identifying the hand in which the manikin held either the square or the circle. The target figure was determined by the geometric figure in which the manikin stood. Thus, if the manikin stood inside a square, the subject responded by identifying the hand in which the manikin held the square. If the manikin stood inside the circle, the subject identified the hand in which the manikin held the circle. In each presentation the manikin appeared in one of the following four orientations: (1) right side up facing toward the subject; (2) right side up facing away from the subject; (3) upside down facing toward the subject; and (4) upside down facing away from the subject. The subject had to mentally rotate the figure in order to identify the hand holding the target geometric figure.

The logical reasoning task consisted of the simultaneous presentation of the letter pair "AB" or "BA" and a statement which correctly or incorrectly described the letter pair (e.g., "A precedes B"). Sentences were worded in the active or passive voice, and there was a negation in some sentences which was absent from others. The subject indicated as quickly as possible whether the statement was an accurate or inaccurate description of the letter pair.

Results

Spontaneous electroencephalogram

Resting EEG data were collected at two different points during each of 14 sessions throughout the investigation. Data were collected from a 5-minute period immediately preceding the mental rotation task and again from a 5-minute period immediately prior to the logical reasoning task. These two periods were separated by approximately 5 to 7 minutes. To simplify the analyses of the EEG, each data set was analyzed in a separate series of two-way analyses of variance (ANOVA) in which the factors were day (day 1, day 2, and day 3) and session (0700,

1300, and 1730). Note that only the sessions which were consistently present during baseline and the 2 deprivation days were included here. Thus, of the 14 sessions total, only 9 sessions were examined in the two-way ANOVAs.

The data analyzed for each session consisted of absolute power values for the delta, theta, alpha, and beta bands at F_2 , C_2 , and P_2 . Also, both coherence and power asymmetry analyses were conducted on the C_3 - C_4 pair, the P_3 - P_4 pair, and the O_3 - O_4 pair of electrodes. The power values were obtained by performing Fast Fourier Transforms on 10 artifact-free, 2.5-second epochs from each subject's record at each of the time periods delineated above. The 10 FFTs were then averaged together to yield one set of power calculations per electrode for each time period. Coherence and asymmetry data were calculated on the same epochs. These data were analyzed with ANOVAs to determine the presence of significant main effects and/or interactions. Subsequent post hoc contrasts were performed to pinpoint the precise nature of any observed effect.

EEG prior to logical reasoning

Delta activity

The two-way ANOVA performed on absolute power within the delta band indicated no interactions and no main effects attributable to session at any electrode. There was a tendency toward Day effect at F_2 (F(1.11, 7.74)=3.86, p=.0842), but none of the post hoc contrasts revealed a difference. There was a tendency towards increased delta between days 1-2 and days 1-3 (p<.07). The means are graphed in Figure 1.

Theta activity

The analysis of theta activity also revealed no interactions and no session main effects, but there were differences attributable to day at C_z (F (2,14)=3.18, p=.0477) and F_z (F(2,14)=4.80, p=.0258). At C_z , none of the contrasts were significant, with only a tendency toward increases from day 1 to day 3 (p<.07). At F_z , however, there was a clear increase in theta from day 1 to day 3 (p<.05). All of these effects may be seen in Figure 2.

Alpha activity

The ANOVA performed on alpha power at each electrode indicated only one significant effect, and this was the day main effect at P, (F(2,14)=3.75,p=.0496). Post hoc contrasts showed

this was due to a significant reduction in alpha activity from day 2 to day 3 (p<.05). See Figure 3. There were no other marked changes.

Beta activity

The two-way ANOVA on absolute power within the beta band at the four midline electrodes revealed there were no significant main effects or interactions.

Coherence

Coherence of the activity within each of the above frequency bands was calculated between three pairs of electrodes as mentioned earlier. These data were examined to understand the effects of sleep deprivation on synchronization of electrical activity between electrode pairs—a 1.0 indicating a high level of functional coordination (100%) between corresponding regions of the two hemispheres and a 0.0 suggesting absolutely no synchronization or coordination (0%) between the two hemispheres.

The two-way ANOVAs of coherence data indicated that there were differences among days only within the delta band between the C_3-C_2 pair (F(2,14)=4.54,p=.0302) and the P_3-P_2 pair (F(2,14)=3.89, p=.0453) -- the O_1-O_2 effect was only marginal (p=.10). Subsequent contrasts for C₃-C₄ coherence revealed a reduction in synchronization of activity from day 1 to day 3 (p<.05), but there were no other differences. Contrasts for P₃-P₄ data also indicated reduced synchrony due to deprivation, however, in this case the difference was between days 1 and 2 (p<.05). Figure 4 presents the data for the three electrode rairs. In addition to these effects on the day factor, there was one difference on the session factor. The session main effect was for the coherence between C3 and C4 within the delta band (F(2,14)=5.37,p=.0185), and subsequent contrasts showed this resulted from increased synchrony at the 1730 session in comparison to both the 1300 session and the 0700 session (p<.05).

Asymmetry

In addition to examining the synchronization of activity from three pairs of electrodes, the symmetry of this activity was assessed as well. These data permit an examination of differences in levels of activity (in the delta, theta, alpha, and beta bands) between homologous electrode pairs—a 1.0 indicating a 100 percent difference in the power of activity between corresponding regions of the two hemispheres and a 0.0 suggesting perfectly balanced power of activity between the two hemispheres. Positive values indicated there was more power in

the left hemisphere, and negative values indicated more power in the right.

The two-way ANOVAs of asymmetry data revealed no significant differences as a function of either day or session within any of the activity bands examined.

EEG prior to mental rotation

Approximately 6 to 7 minutes after the resting EEG discussed above, there was another 5-minute EEG. By this time, the subject had been seated in the testing chamber for several minutes, and he had completed the logical reasoning task which was approximately 6-7 minutes in length.

Delta activity

The ANOVA performed to examine delta activity at the midline electrodes during this rest period revealed no interactions or session effects. However, there were day effects found at F, (F(2,14)=3.67,p=.0522). Contrasts indicated the effect was due to an increase in delta activity from day 1 to day 3 (p<.05), but none of the other comparisons were significant. The increased delta activity is depicted in Figure 5.

Theta activity

The analysis of theta activity again revealed no interactions or main effects attributable to session, but as was the case earlier, there were differences attributable to day. There were significant day main effects at F_z (F(2,14)=6.44, p=.0104), C_z (F(2,14)=6.22, p=.0117), and P_z (F(2,14)=5.95, p=.0135). At all three electrodes, the day effect resulted from increases in theta from days 1-3 (p<.05), and at C_z and P_z there were increases from days 1-2 as well (p<.05). These effects are presented in Figure 6.

Alpha activity

The analysis of alpha activity revealed no changes attributable to sleep deprivation (day) or time of day (session). Also, there was no interaction.

Beta activity

As was the case with alpha activity, there were no changes in beta activity as a function of either day or session.

Coherence

The analysis of synchronization of activity from homologous electrodes indicated a significant difference in the C_3 - C_4 pair within only the delta band as a function of day (F(2,14)=5.06, p=.0222). This effect was a result of the decreased synchrony of delta activity from day 1 to day 3 (p<.05). None of the other comparisons were significant (there were only slight tendencies of p<.20). The impact of sleep deprivation on these data is shown in Figure 7. With regard to the impact of time of day, there was only a single session main effect which was found within the alpha band for the C_3 - C_4 pair (F(2,14)=4.12,p=.0391). This was because of less synchronization at 1300 than at 0700 (p<.05)--an effect somewhat similar to the one found in delta activity prior to the logical reasoning task.

Asymmetry

The ANOVAs on the differences in power between homologous electrode pairs within each activity band revealed main effects attributable to day for theta. Sleep deprivation significantly altered the symmetry of theta activity for the C_3 - C_4 electrode pair (F(2,14)=5.80,p=.0146), the P_3 - P_4 pair (F(2,14)=3.80, p=.0481), and the O_1 - O_2 pair (F(2,14)=6.15,p=.0121). Contrasts for the C_3 - C_4 data revealed increased differences in theta asymmetry between days 1-3 and days 2-3 (p<.05). The P_3 - P_4 data indicated greater amounts of theta asymmetry on day 2 than on day 1 (p<.05) but only a marginal (p=.07) difference between days 1 and 3. The O_1 - O_2 data revealed increased theta asymmetry from day 1 to day 2 and day 1 to day 3 (p<.05). In all of these cases, the asymmetry was characterized by reductions in theta in the left hemisphere as compared to the right hemisphere. The data is depicted in Figure 8.

Middle latency evoked response (MLR) data

Prior to the PAB tests, MLR data were collected during every session in close proximity to the EEG recording. These evoked responses were examined in a number of ways to include the following: 1) latency, 2) amplitude, 3) morphology of waveforms from 21 electrodes, 4) area under the curve, 5) root mean square (RMS), and 5) power of 10 Hz activity (via FFT calculations).

MLR latency

MLR components from F_z were scored in terms of latency across days and sessions. These data then were analyzed using a

two-factor analysis of variance (day by session). The analysis of data from days 1 (rested), 2 (first deprivation day), and 3 (second deprivation day) at the 0700, 1300, and 1730 sessions, revealed no significant day by session interactions or session main effects. The only significant change in latency was detected as a main effect of day on the Pa component (F(2,14)=3.70;p=.0513). The largest mean latency differences were found between day 1 (33.25 ms) and day 3 (34.67 ms) and day 2 (33.29 ms) and day 3. These may be compared to the latencies of MLR components after a normal night of sleep (presented in Table 5).

MLR amplitude

A similar two-way factorial ANOVA was applied to F, amplitude data across days 1, 2, and 3 from the 0700, 1300, and 1730 sessions. This analysis revealed no significant day by session interactions, session main effects, or day main effects. However, P1 amplitudes exhibited a tendency to increase on both sleep deprivation days (Figure 9), but this was not statistically significant (F(2,14)=2.85;p=.0916).

MLR morphology

To visually assess the general changes in latency and amplitude across the remaining 20 electrodes (in addition to F.), sequential mapping of amplitudes was conducted on MLR latencies starting at 35 ms using 5 ms increments. This strategy permitted a further examination of the amplitude changes associated with the Nb-P1 complex and subsequent components. In Figure 10 (Panels I-IV), waveforms in all electrode locations were plotted across days for one subject. Examination of the Nb-Pl complex over midline electrode locations indicates an apparent increase in amplitude of the P1 component and an increase in the time required for the voltage to recover to baseline values after the positive excursion. This prolonged positivity was more evident in the corresponding sequential mapping of voltage shown on Figure 11A (Panels I-IV). Note the increase in voltage over the frontomedial locations at latencies of 50, 55, and 60 ms which can be observed when baseline maps are contrasted to the maps from 24 and 48 hours of continued wakefulness, see Figure 11A (Panels I-IV). This increase in positive voltage persists up to 65 ms (Figure 11A: Panels I-IV). In contrast, recovery maps exhibit a noticeable decrease in amplitude at 60, 65, and 70 ms. This return to baseline values (in the recovery maps) indicates a fast recovery cycle of the P1 component after only one period of

sleep (12-14 hours). This fact can be further appreciated by comparing P1 components of time histories at F, across conditions, see Figure 10 (Panels I-IV). Similar changes in amplitude over frontomedial sites are depicted in Figure 11B (Panels I-IV).

Examination of sequential maps was conducted for all subjects (1 through 8) and revealed similar patterns of changes, namely increased positivity spreading into latencies above 60 ms. These observations indicated that the area under the curve between 40 to 70 ms appeared to increase during deprivation. To verify this finding statistically, additional analyses were conducted.

MLR Area, RMS, and 10 Hz

Area, RMS, and 10 Hz absolute power data were analyzed separately in a series of two-way analyses of variance in which the same three sessions (0730, 1300, and 1730) on each day (1, 2, and 3) were included. Thus, there were six ANOVAs (Area, RMS, and FFT for both F_z and C_z) which were conducted on 9 of the 14 test sessions. The few instances of missing data were handled by substituting the means of the existing data using BMDPAM.

The area, RMS, and FFT calculations were carried out on two sets of data--one examined the waveforms from 20 to 100 ms and the other examined waveforms from 40 to 100 ms. Since there were no significant differences in the results from the two sets of analyses, only the results from the 40 to 100 ms data set will be reported. The fast Fourier transformation (FFT) was used to calculate absolute power under the 10 Hz component. This was the only frequency analyzed since the positivity associated with sleep deprivation exhibited a slow recovery cycle which did not exceed 10 Hz.

Analysis of F, data from days 1-3

The analyses of the data collected from F_z indicated there was not a significant day-by-session interaction or session main effect for any of the scores. However, there were day main effects for Area (F(2,14)=17.60, p=.0002), RMS (F(2,14)=16.35, p=.0002), and FFT (F(2,14)=9.16, p=.0029) scores (Figures 12, 13, and 14). In every case, there were differences between days 1 and 2 and days 1 and 3 (Table 6). This analysis scheme was applied to data obtained from midline electrode locations, namely F_z , C_z , P_z , and O_z . Examination of the means revealed that the area under the curve was increased between the undeprived day and the two sleep-deprived days. Also, both RMS values and 10 Hz power values were elevated in a similar way (Table 7).

Analysis of C, data from days 1-3

The analyses of the data collected from Cz also indicated that there were no day by session interactions or session main effects. However, once again, there were differences attributable to the day factor on Area (F(2,14)=20.99,p=.0001), RMS (F(2,14)=23.32,p<.0001), and FFT (F(2,14)=20.59,p=.0001). In every case, there were significant differences between days 1 and 2 and between days 1 and 3 (Table 8). Inspection of the means across days revealed that, as with the data from F, there were significant elevations in all of the values from the undeprived to the deprived days. The means are presented in Table 9.

Analyses of F, and C, data from days 1-4

One other set of analyses was conducted on these data in order to determine whether the effects which occurred as a function of sleep deprivation would dissipate on the recovery day (day 4). For these analyses only the 1300 sessions were used, but in addition to days 1, 2, and 3, the data from the 4th day was added (only the 1300 session was collected on the 4th day). Then, a one-way analysis of variance was conducted on Area, RMS, and FFT at both F, and C,.

The results of this analysis indicated there were day effects for Area at F_z (F(3,21)=5.83,p=.0046), RMS at F_z (F(3,21)=5.18,p=.0078), and FFT at F_z (F(3,21)=3.64,p=.0295). Also, there were day effects for Area at C_z (F(3,21)=5.53, p=.0059), RMS at C_z (F(3,21)=5.21,p=.0076), and FFT at C_z (F(3,21)=5.17,p=.0078). Subsequent contrasts showed that these effects were due to differences between day 1 and day 3 for every measure. There were also differences between days 2 and 4 for every measure with the exception of FFT at F_z , and there were differences between days 3 and 4 for every measure. Significance levels for the contrasts are presented in Table 10. Means are presented in Table 11.

Inspection of these means shows that in every case there were increases associated with sleep deprivation (days 2 and 3). However, after recovery sleep (day 4) all of the values tended to return to baseline levels.

Performance assessment battery results

Cognitive performance was assessed approximately every 4 hours throughout the sleep deprivation period and once at 1300 on the recovery day. This resulted in 14 cognitive data

collection sessions during the course of the study. However, only a subset of these sessions was analyzed. Mental rotation and logical reasoning data were submitted to separate two-way repeated measures analyses of variance with three levels for the day factor (day 1, day 2, and day 3) and three levels for the session factor (0700, 1300, 1730). Significant effects were explored using linear contrasts. The dependent variables for both the mental rotation and logical reasoning analyses were the mean reaction time (RT) for correct responses and the transformed percent correct. The percent correct values were transformed using:

2 arcsine √x

where x is the percent correct value converted to a proportion.

Results of the analysis for the mean RT for correct responses on the mental rotation task revealed no interaction. However, there was a significant day main effect (F(2,14)=8.39, p=0.0040) and a significant session main effect (F(2,14)=6.35, p=0.0109) (Figures 15 and 16). Contrasts for the day main effect indicated RTs increased significantly after 55 hours deprivation relative to both baseline and 31 hours of sleep deprivation. Contrasts for the session main effect indicated that RTs improved significantly throughout the day from 0700 to 1730 (Figure 16). Results of the analysis for the transformed percent correct on the mental rotation task indicated there were no significant changes in accuracy of performance as a function of sleep deprivation.

Analyses for the same measures on the logical reasoning task revealed no significant effect on any measure. The mean RT for correct responses on the logical reasoning task displayed essentially the same pattern as on the mental rotation task, but subject variability was greater, perhaps a result of individual differences in solution strategy for the logical reasoning task (Clark and Chase, 1972). As with mental rotation, there were no changes in accuracy of performance on the logical reasoning task as a function of sleep deprivation.

Discussion

While PAB data showed no significant changes until after 55 hours of sleep deprivation, EEG and MLR data showed significant changes after only 24 hours of continuous wakefulness. Generally, the electrophysiological results provided early and convincing evidence of central nervous system degradation.

There were changes in EEG coherence and asymmetry which suggested cortical functional degradation during both deprivation days. Prior to logical reasoning sessions, delta coherence between P, and P, decreased on the first deprivation day, delta coherence between C, and C, decreased by the second day of These effects may have been particularly severe at the 0700 and 1300 sessions where it was observed that regardless of sleep deprivation, delta coherence was lower than at 1730. Somewhat similar effects were observed immediately prior to the mental rotation task (a few minutes later) where there was again reduced delta coherence at the C3- C4 pair by the second day of deprivation. The deterioration suggested by coherence reductions was partially confirmed by the existence of concurrent asymmetries. There were increases in the asymmetry of theta activity found between C_3 and C_4 and P_3 and P_4 as a function of sleep deprivation. In general, both the coherence and asymmetry effects are of interest because they may indicate the deterioration of cortical functional integrity as a function of sleep deprivation.

There were also significant changes in the frequency of the EEG because of sleep deprivation. Generally, there was a slowing of activity evident on the first day of deprivation which continued throughout the second day as well. Spontaneous delta activity prior to the logical reasoning test tended to increase on both days, and theta was significantly elevated by the second day of deprivation. Meanwhile, absolute power in the alpha band was reduced. A few minutes later, prior to the mental rotation task, both delta and theta activity were substantially elevated on the second day of deprivation, and theta increases were observed after the loss of a single night of sleep.

These changes in the EEG are supportive of the findings of earlier investigators. The reductions in alpha activity have been observed in numerous sleep deprivation studies (summarized in Horne, 1978); thus, the finding of alpha suppression was an expected outcome in the present investigation. Increases in slow-wave activity (delta and theta) have been less often reported, but Pigeau, Heslegrave, and Angus (1987) reported elevations in both delta and theta concurrent with alpha suppression in a study of the effects of 64 hours without sleep. Thus, our findings are in agreement with earlier reports. As a further point of interest, it should be noted that these types of EEG changes have been found to be associated with degrading task performance in both sleep deprivation studies (Pigeau et al., 1987) and short-term vigilance studies (Belyavin and Wright, 1987).

Increased EEG slowing with concurrent alpha suppression represents an essential feature of the transition into stage 1 of sleep. The subjects were continuously monitored by staff members and were reported to have remained behaviorally awake (eyes open) during test sessions, but transitions into sleep were likely to have occurred during both the EEG and MLR recording sessions. The electrophysiological data suggest that despite behavioral evidence of wakefulness, the subjects were only marginally alert.

Changes in MLR components provided evidence of CNS functional changes throughout both sleep deprivation days. Pa latency and Pl amplitude increased at F, as a function of progressive sleep loss. Increased area under the curve (Nb-Pl), elevated power in the 10 Hz frequency band, and increased RMS characterized general changes in the morphology of the MLR time history. These effects were observed on the first day of deprivation, persisted throughout the second day, and returned to baseline (undeprived) after one night of recovery sleep.

Slower recovery periods of the P1 component at F, (area of the time history from 40 to 100 ms) observed during both the first and second day of sleep deprivation could not be predicted from existing experimental data (Erwin and Buchwald, 1986). In contrast to the previously reported disappearance of the P1 component during slow wave sleep, P1 was clearly visible during both days of sleep deprivation.

For each subject, area and RMS measurements could be used to track changes in the area under the curve between 40 to 100 ms throughout the sessions on undeprived day 1 (0700, 1300, 1730, and 2200) and the sessions on deprived days 2 and 3 (0700, 1300, 1730, 2200, and 0300) as can be seen in Figures 17-24. Similarly, FFT data indicated that the changes in the Nb-Pl complex may be associated with a slow positive component with a center frequency at 10 Hz. Figures 25 through 32 show that increments of absolute 10 Hz power above two standard deviations from the baseline means were first observed at 24 hours of continuous wakefulness (subjects 1, 2, 4, 6, and 8).

During sleep deprivation, the presence of a slow positive potential over the MLR time history may indicate a significant slowing in the recovery cycle of the P1 component and may be indicative of degraded alertness. However, this finding also suggests that a stimulus-locked slow positive potential which affects the morphology of the slowest MLR component (P1) may be associated with changes in neural activity due to sleep deprivation.

FFT analysis of the MLR time history revealed that the absolute power under the 10 Hz component (bandwidth 5 to 15 Hz) increased significantly during sleep deprivation (Figure 12). Both the theta and MLR changes began to occur after approximately 24 hours of continuous wakefulness, but whether the change in one index was related to the change in the other is not certain. However, the possibility that theta activity may influence the morphology of the Nb-P1 complex must be examined before attributing these results to an effect of sleep loss on the neural substrates of the human MLR.

In general, three possible alternative explanations can be formulated with regard to the effects of sleep deprivation on the MLR: 1) a slow positive potential is associated with degraded alertness, but it is not generated by the neural substrates responsible for MLR components; 2) changes in P1 morphology reflect functional changes of the MLR generating system as a function of sleep deprivation; and 3) increased theta activity during sleep deprivation affects the morphology of averaged MLR components, particularly the P1 component. Additional investigations will be required to determine the relevance of these alternatives.

In the meantime, it is evident that both the spontaneous EEG and the middle latency evoked response are particularly sensitive to the effects of sleep deprivation in human subjects. However, limited measures of cognitive performance appear to be less vulnerable to deprivation effects especially in the early stages.

Conclusions

The results from the MLR-EEG-PAB test profile yielded data indicating that sustained wakefulness adversely affected CNS function from the first night of sleep deprivation, but it did not impact performance in a cognitive mental rotation task until after the second night. Performance in the logical reasoning task appeared unaffected by sleep deprivation. Apparently, in the first 48 hours of sleep loss, subjects were able to compensate for the adverse effects of fatigue in each cognitive test session, whereas they were unable to do so later. Performance in the mental rotation task did not show significant degradation until the 0700 session of the second day of sleep deprivation.

In contrast, electrophysiological dependent measures indicated increased drowsiness (delta and theta increases with alpha suppression), CNS functional degradation (loss of coherence

and increased asymmetry), and slower processing of sensory stimuli (slower recovery of the MLR P1 component) after the first night of sleep deprivation (after approximately 24 hours of continuous wakefulness). Both cognitive and electrophysiological variables showed concurrent changes as a function of sustained wakefulness at the 0700 test session on the second day of sleep deprivation.

Although these results are encouraging in that the MLR-EEG-PAB profile does characterize the status of some aspects of CNS and cognitive function during sleep deprivation, it may be necessary to explore the use of more sensitive cognitive assessment tests. Both the logical reasoning and mental rotation tests were subject-paced in this investigation. Therefore, participants had the option to trade reaction time for accuracy. Throughout sessions, reaction times degraded slowly always showing a trend across sessions but not reaching significantly greater values until the second day of deprivation. It is possible that using machine-driven cognitive tests with preset trial durations will prevent the trade of accuracy for reaction time. This may result in the detection of degradation of both variables during the first night of sleep deprivation.

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Appendix A
Tables

Table 1.

Adaptation day

Day 0	
0700-0800 0800-1100	Breakfast b. Electrode application c. Test: MLR-PAB-EEG
1130-1230 1300-1500 1600-1700 1700-1900 2200-2400	Lunch Test: EEG-PAB-MLR Dinner Test: EEG-PAB-MLR Test: EEG-PAB-MLR

Table 2.
Baseline testing schedule

Day 1	
0545	Wake-up
0600-0700	Breakfast
0700-1000	Test: EEG-PAB-MLR
1130-1230	Lunch
1300-1500	Test: EEG-PAB-MLR
1600-1700	Dinner
1700-1900	Test: EEG-PAB-MLR
2200-2400	Test: EEG-PAB-MLR

Table 3. Sleep deprivation testing schedule

Day 2	
0300-0500	Test: EEG-PAB-MLR
0600-0700	Breakfast
0700-1100	Test: EEG-PAB-MLR
1130-1230	Lunch
1300-1500	Test: EEG-PAB-MLR
1600-1700	Dinner
1700-1900	Test: EEG-PAB-MLR
2200-2400	Test: EEG-PAB-MLR
Day 3	
0300-0500	Test: EEG-PAB-MLR
0600-0700	Breakfast
0700-0900	Test: EEG-PAB-MLR
1130-1230	Lunch
1300-1500	Test: EEG-PAB-MLR
1600-1700	Dinner
1700-1900	Test: EEG-PAB-MLR
2200-2400	Test: EEG-PAB-MLR
	Subjects slept

Table 4.
Recovery test schedule

Day 4	
1100	Waka-un
1130-1230	Wake-up Lunch
1300-1500	Test: EEG-PAB-MLR

Table 5.

MLR latencies

(*)	Na	Pa	Nb	P1
Mean(SD)	21.03(1.8)	35.18(4.9)	45.22(7.6)	61.83(5.6)

(*)averaged across all subjects over four sessions recorded prior to sleep deprivation

Table 6.
Contrasts for the day effects at Fz

			*=========
Measure	Day 1 vs 2	Day 1 vs 3	Day 2 vs 3
Area	F=13.93;p<.01	F=32.24;p<.01	ns
RMS	F=14.49;p<.01	F=26.21;p<.01	ns
FFT	F=07.28; p=.03	F=14.30;p<.01	ns

Table 7.

Means for the day effects at Fz

Day	Area	RMS	FFT			
1	63.96	0.93	264.79			
2	91.54	1.31	366.20			
3	96.23	1.36	393.28			

Measure	Day 1 vs 2	Day 1 vs 3	Day 2 vs 3
Area	F=19.91;p<.01	F=32.58;p<.01	ns
RMS	F=24.64; p<.01	F=33.04;p<.01	ns
FFT	F=21.46; p=.03	F=31.87;p<.01	ns

Table 9. Means for the day effects at Cz

Day	Area	RMS	FFT	
1	53.25	0.78	207.25	
2	85.79	1.24	344.83	
3	89.95	1.29	361.44	

Table 10.

Contrasts for the day effects (days 1-4)

=======						======
Measure	Day 1-2	Day 1-3	Day 1-4	Day 2-3	Day 2-4	Day 3-4
Fz area Fz RMS Fz FFT Cz area Cz RMS Cz FFT	p=.10 p=.11 p=.35 p=.06 p=.06 p=.10	p<.02 p<.02 p<.03 p<.04 p<.05 p<.05	p=.40 p=.59 p=.93 p=.61 p=.75 p=.89	p=.27 p=.30 p=.17 p=.36 p=.44 p=.26	p<.05 p<.05 p=.18 p<.02 p<.01 p<.02	p<.01 p<.01 p<.01 p<.02 p<.02 p<.02

Table 11.

Means for the day effect (days 1-4)

Measure	Day 1	Day 2	Day 3	Day 4
Fz area	62.50	87.25	100.43	68.88
Fz RMS	0.93	1.24	1.42	0.99
Fz FFT	275.88	342.75	420.71	279.75
Cz area	50.00	78.12	87.71	55.00
Cz RMS	0.76	1.13	1.25	0.80
Cz FFT	210.75	311.50	364.57	217.75

Appendix B Figures

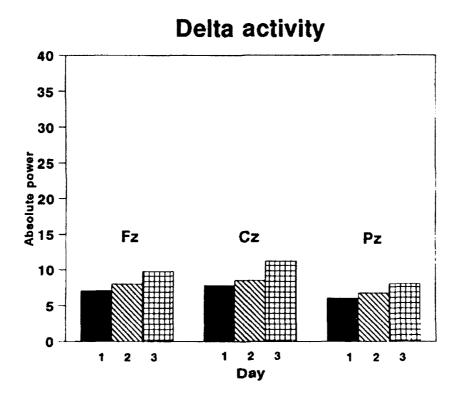


Figure 1. Delta activity prior to the logical reasoning task.

Average delta absolute power recorded during baseline (day 1), 24 hours sleep deprivation (day 2), and 48 hours sleep deprivation (day 3).

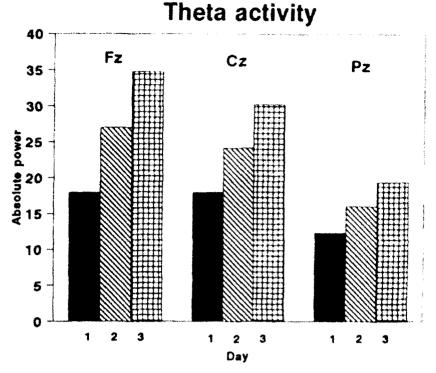


Figure 2. Theta activity prior to the logical reasoning task.

Average theta absolute power recorded during baseline (day 1), 24 hours sleep deprivation (day 2), and 48 hours sleep deprivation (day 3).

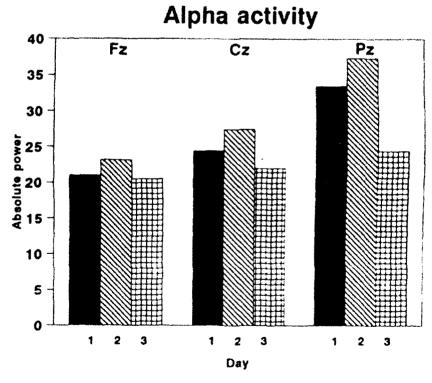


Figure 3. Alpha activity prior to the logical reasoning task.

Average aplha absolute power recorded during baseline (day 1), 24 hours sleep deprivation (day 2), and 48 hours sleep deprivation (day 3).

Delta coherence

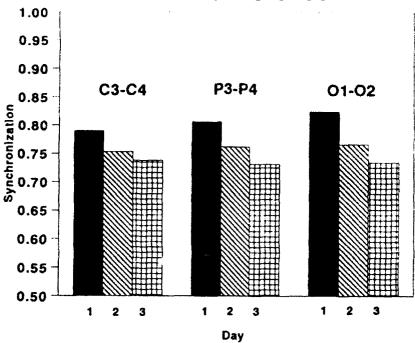


Figure 4. Delta coherence prior to the logical reasoning task. Synchronization of delta activity between the C3-C4 pair, the P3-P4 pair, and the O1-C2 pair during baseline (day 1), 24 hours sleep deprivation (day 2), and 48 hours sleep deprivation.

Delta activity

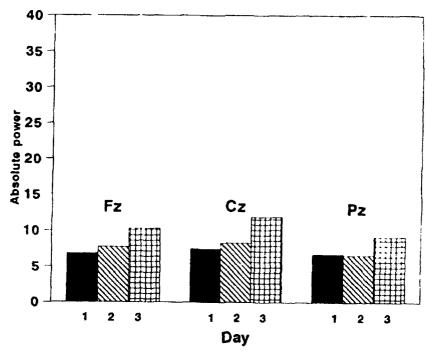


Figure 5. Delta activity prior to the mental rotation task.

Average delta absolute power recorded during
baseline (day 1), 24 hours sleep deprivation (day 2),
and 48 hours sleep deprivation (day 3).

Theta activity

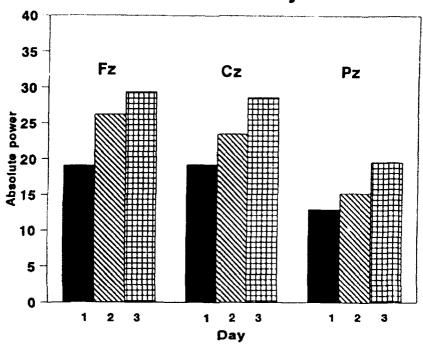


Figure 6. Theta activity prior to the mental rotation task.

Average theta absolute power recorded during baseline (day 1), 24 hours sleep deprivation (day 2), and 48 hours sleep deprivation (day 3).

Delta coherence

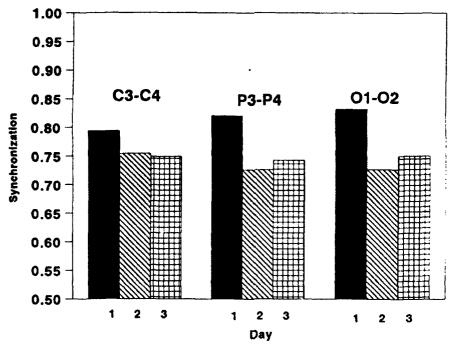


Figure 7. Delta coherence prior to the mental rotation task. Synchronization of delta activity between the C3-C4 pair, the P3-P4 pair, and the 01-02 pair during baseline (day 1), 24 hours sleep deprivation (day 2), and 48 hours sleep deprivation (day 3).

Theta asymmetry

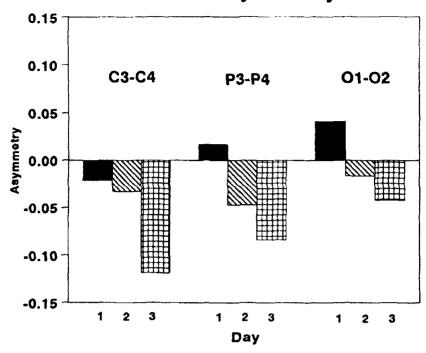


Figure 8. Theta asymmetry prior to the mental rotation task.
Asymmetry of theta activity for the C3-C4 electrode pair, the P3-P4 pair, and the O1-O2 pair during baseline (day 1), 24 hours sleep deprivation (day 2), and 48 hours sleep deprivation (day 3).

Means for day effect P1 amplitude

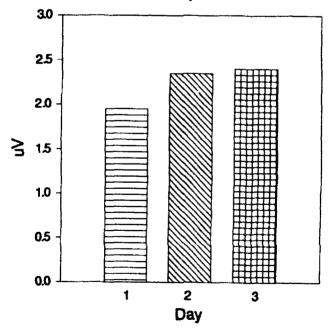


Figure 9. P1 amplitude: Means for the day effect.
Fz amplitudes over days 1 (rested), 2 (first deprivation day), and 3 (second deprivation day).

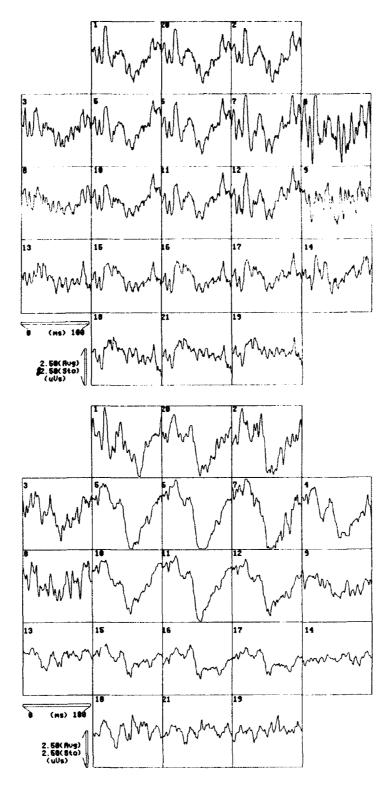


Figure 10. Examination of the Nb-Pl complex over midline electrode locations starting at 35 ms using 5 ms increments during baseline, 24 hours sleep deprivation, 48 hours sleep deprivation, and recovery. (Panels I-II)

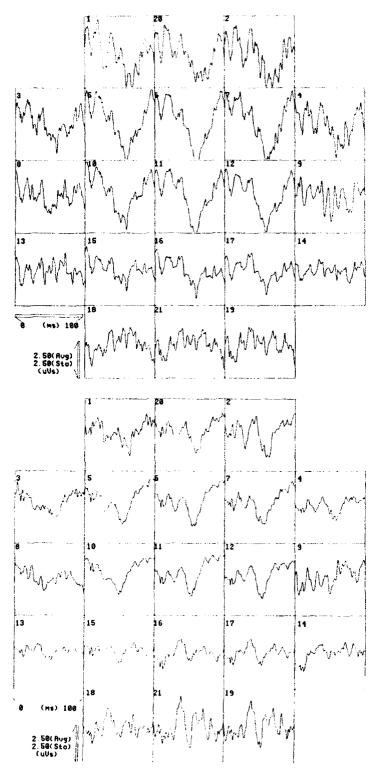


Figure 10. Examination of the Nb-Pl complex over midline electrode locations starting at 35 ms using 5 ms increments during baseline, 24 hours sleep deprivation, 48 hours sleep deprivation, and recovery. (Panels III-IV)

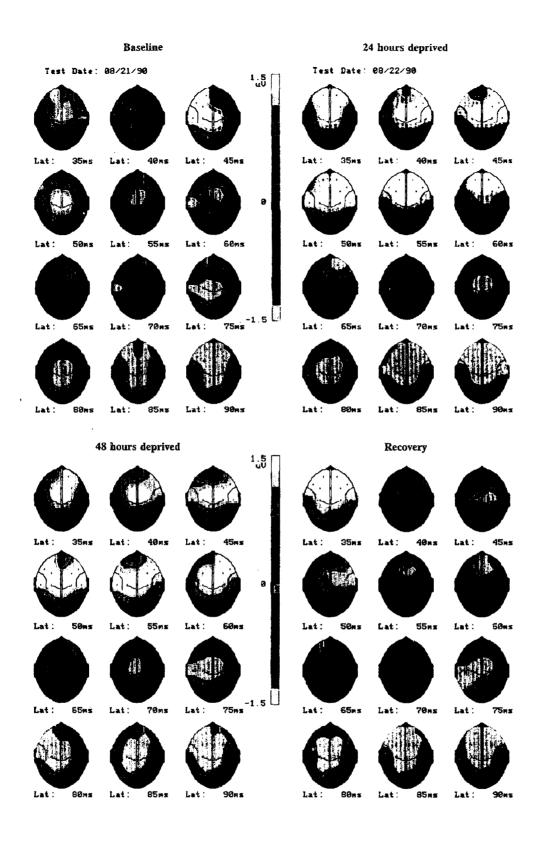


Figure 11A. Comparison of positive voltage over frontomedial locations (baseline maps at 50, 55, and 60 ms are contrasted to respective latencies at 24 and 48 hours of continued wakefulness (Panels I-IV).

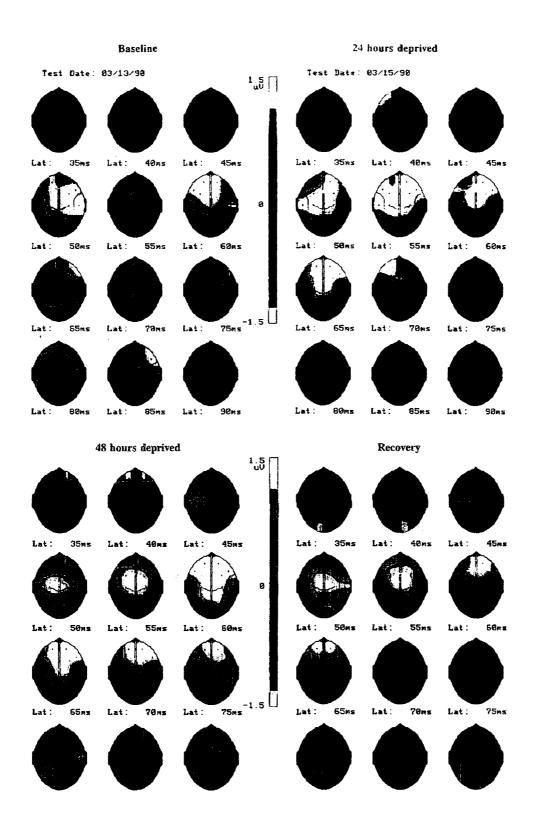


Figure 11B. Comparison of positive voltage over frontomedial locations (baseline maps at 50, 55, and 60 ms are contrasted to respective latencies at 24 and 48 hours of continued wakefulness (Panels I-IV).

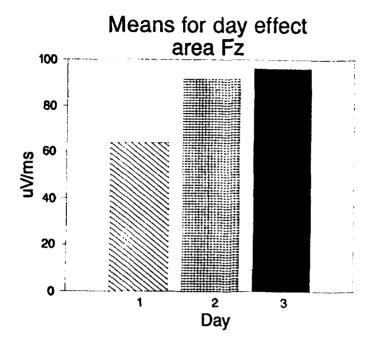


Figure 12. Means for the day effect on area at Fz during baseline (day 1) and two days of sleep deprivation (days 2 and 3).

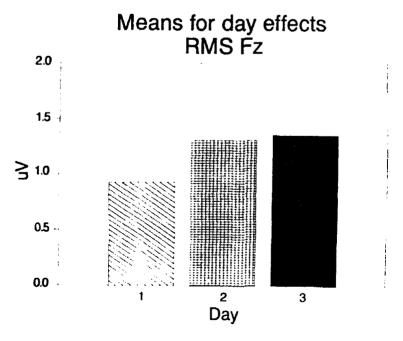


Figure 13. Means for the day effect on RMS at Fz during baseline (day 1) and two days of sleep deprivation (days 2 and 3).

Figure 14. Means for the day effect on 10-Hz FFT at Fz during baseline (day 1) and two days of sleep deprivation (days 2 and 3).

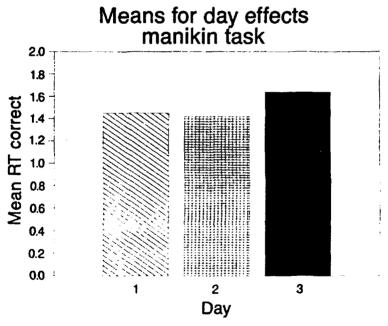


Figure 15. Means for the day effect on mean reaction time for correct responses in the manikin task during baseline (day 1) and two days of sleep deprivation (days 2 and 3).

Means for session effect manikin task

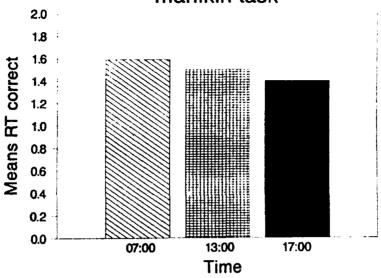


Figure 16. Means for the session effect on mean reaction time for correct responses in the manikin task at 0700, 1300, and 1730 h sessions.

Subject 1

MLR area

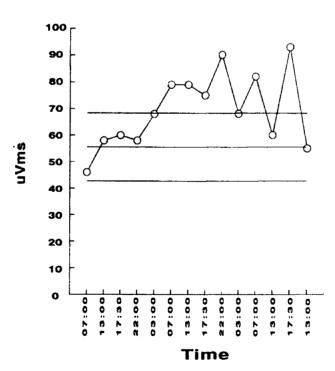


Figure 17. Subject 1. Area measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

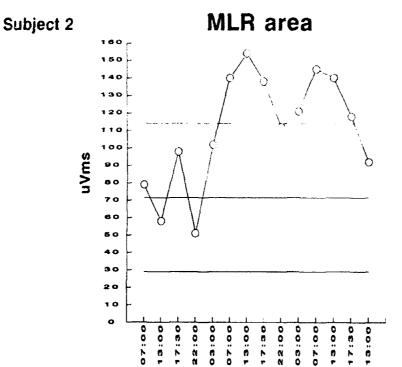


Figure 18. Subject 2. Area measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

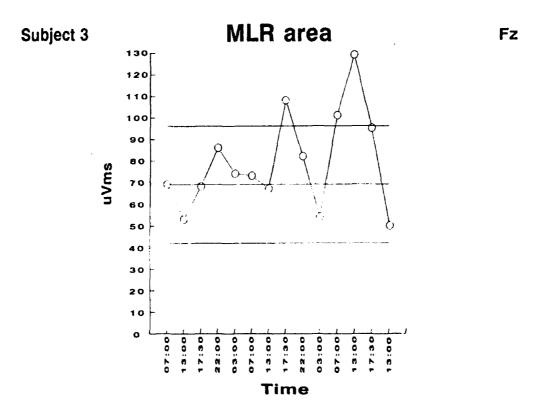


Figure 19. Subject 3. Area measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

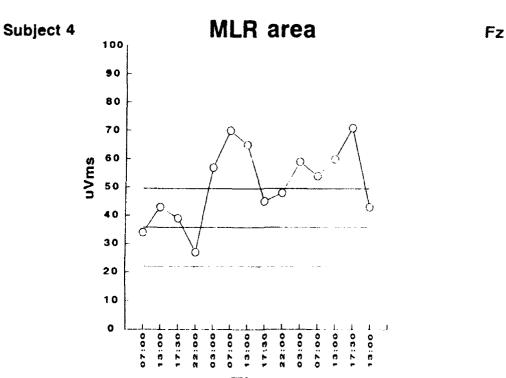


Figure 20. Subject 4. Area measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

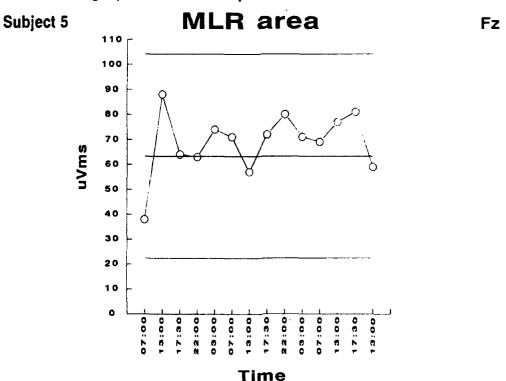


Figure 21. Subject 5. Area measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

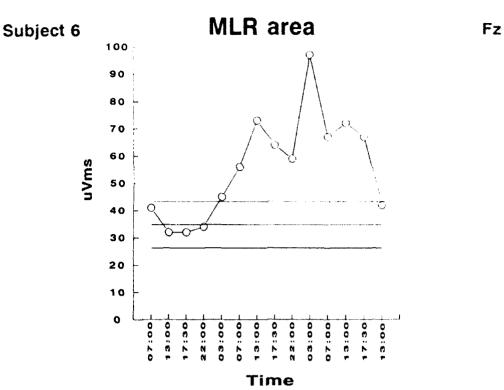


Figure 22. Subject 6. Area measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

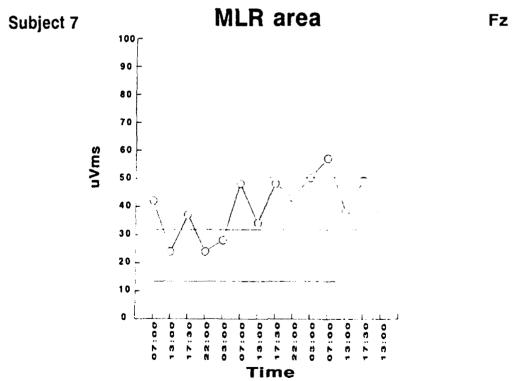


Figure 23. Subject 7. Area measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

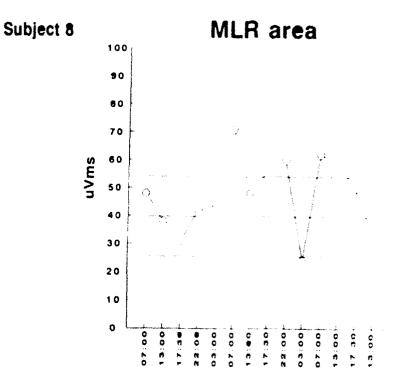


Figure 24. Subject 8. Area measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

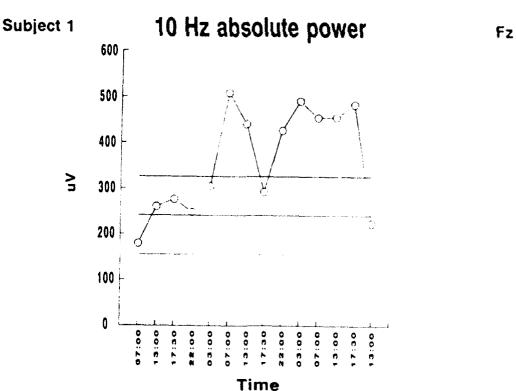
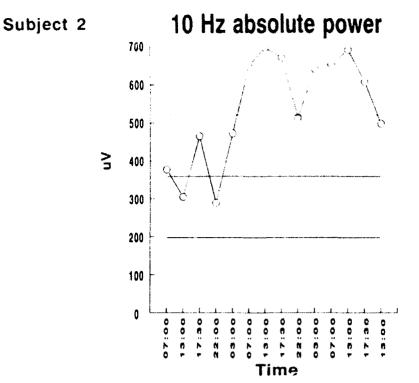


Figure 25. Subject 1. 10 Hz absolute power measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).



Fz

Figure 26. Subject 2. 10 Hz absolute power measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

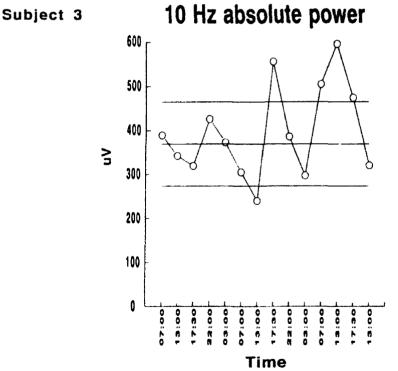


Figure 27. Subject 3. 10 Hz absolute power measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).



10 Hz absolute power

Fz

Fz

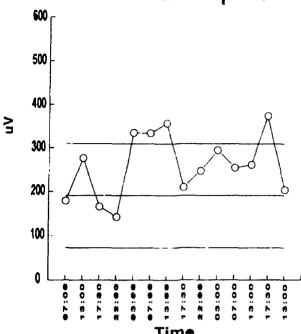


Figure 28. Subject 4. 10 Hz absolute power measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

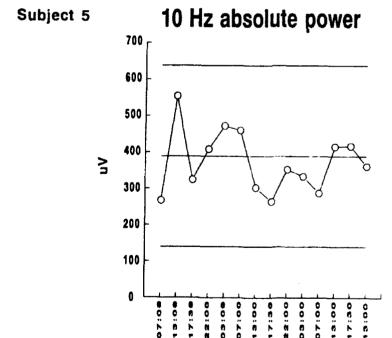


Figure 29. Subject 5. 10 Hz absolute power measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

Time

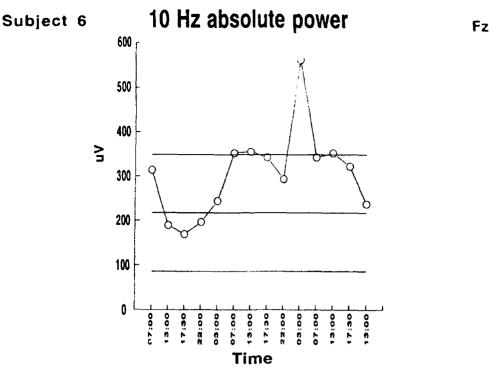


Figure 30. Subject 6. 10 Hz absolute power measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

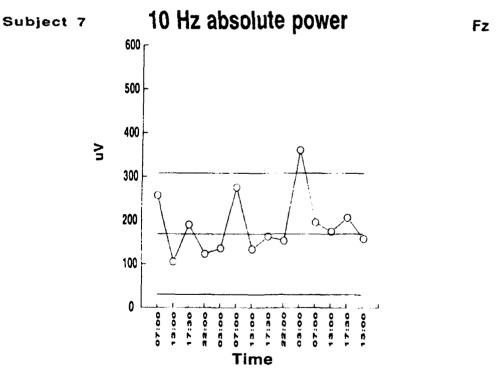


Figure 31. Subject 7. 10 Hz absolute power measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

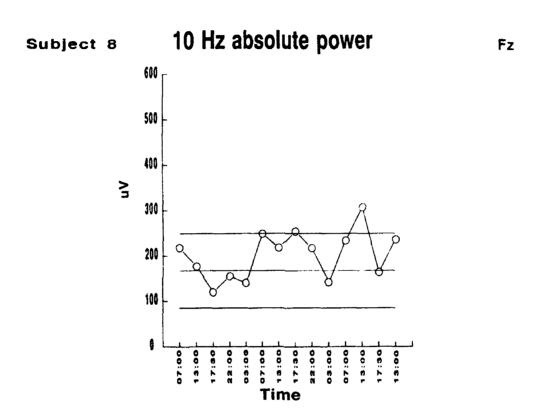


Figure 32. Subject 8. 10 Hz absolute power measurements between 40 and 100 ms throughout undeprived sessions (1st-4th), deprived sessions (5th-13th), and after approximately 12 hours sleep (14th session).

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